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Cheese currently suffers from an adverse nutritional image largely due to a perceived association between saturated fatty acid, cholesterol and the salt content of cheese with cardiovascular disease. However, cheese is also a rich source of essential nutrients such as, proteins, lipids, vitamins and minerals that play an integral part of a healthy diet. This review outlines the composition, structure and physiological characteristics of the nutritionally significant components of cheese, whilst presenting some of the controversies that surround the role of cheese in dietary guidelines and the potential cheese has to improve health in the UK population.

Keywords: Cheese, cardiovascular disease, healthy diet, essential nutrients, salt.

Introduction

Cheese is a nutritious food made mostly from the milk of cows, buffaloes, sheep or goats and is an important component of the UK diet. In the UK, cheese consumption has increased by 10.7% from 5.6 kg to 6.2 kg per head per annum over the last decade; and of all the raw milk produced in the UK in 2008, 26.9% went into the production of cheese (DairyCo 2009). Cheddar cheese, made from cow's milk, is by far the most popular variety of cheese in the UK. In 2008, 204,251 tonnes of Cheddar cheese were sold representing 54.3% of all cheese sales (DairyCo 2009). Therefore, Cheddar cheese can be used as a suitable model to consider the impact of cheese on the UK diet in this review. Although the exact nutritional composition of all cheese types is determined by numerous factors, such as the type of milk used (Species, breed, stage of lactation and fat content) and ripening processes used, most ripened

cheeses contain up to ten times the amount of water-insoluble components compared to milk (Kosikowski and Mistry 1997). For example, in Cheddar about 80 % of the fat and 70 % of the protein in the original milk are increased in the cheese to approximately 32 % and 23 % respectively, making cheese a dairy product of high nutritional value. Despite this, cheese suffers from an adverse nutritional image largely due to a perceived association between saturated fatty acids (SFAs), cholesterol and the salt content of cheese with cardiovascular disease (CVD). For example, the British Heart Foundation recommends limiting the intake of foods high in saturated fat and cholesterol, such as high fat dairy products, to reduce the risk of CVD (British Heart Foundation 2009); and the UK Food Standards Agency's "Eatwell plate", recommends eating cheese less often or consuming smaller portions, with an emphasis on low-fat dairy foods (Food Standards Agency 2009). However, these guidelines do not take into consideration that different types of fats have different health effects and that not all saturated fats within foods, such as cheese, elevate plasma cholesterol to the same extent (Erkkila *et al.* 2008). Furthermore, other fat components within cheese might be considered to be of dietary benefit and health promoting value. These include short chain fatty acids and certain trans fatty acids, which may protect against CVD (Houston *et al.* 2008). In addition, cheese is also a rich source of other essential nutrients such as, proteins, vitamins and minerals that have the potential to play an integral part of a healthy diet in the UK population. Therefore, this review sets out to re-address the image of cheese by outlining the composition, structure and physiological characteristics of the nutritionally significant components of cheese and highlighting the potential cheese has to improve health in the UK population, whilst presenting some of the controversies that surround the role of cheese in dietary guidelines.

Fat

The fat content of cheese varies considerably depending on the milk composition (i.e. fat to protein ratio) and the method of cheese-making used, which essentially controls the fat and protein content of the cheese. This is important because the ratio of fat to protein will affect firmness, mouthfeel, texture and the flavour qualities of cheese (Guinee and McSweeney 2006). In addition, the fat content of cheddar cheese (see Table 1) makes a considerable contribution to its overall nutritional properties. For example, fat is the most valuable source of energy (37 kJ/g) in food and can also provide essential fatty acids that the body can't make itself. However, increasing sedentary lifestyles amongst the UK population has resulted in some individuals consuming an excessive amount of energy in relation to the amount of energy they use, which is a risk factor for overweight and obesity (Lean *et al.* 2006). A number of studies (Brousseau and Schaefer 2000; Mann *et al.* 1997) have also shown that consuming too much fat, particularly SFAs, may increase plasma cholesterol levels in the body which has been associated with increased risk of CVD (Wang 2007). This is significant as CVD is the main cause of death in the UK and accounts for more than one in three deaths, almost 200,000 deaths each year (British Heart Foundation 2008). However, it is now recognised that not all saturated fats in cheese have the same hypercholesterolemic effect.

The bulk of fats in cheese (>95%) are triglycerides, molecules consisting of three fatty acid chains esterfied to a glycerol backbone. Fatty acids are classified according to the number of carbon double bonds they contain. Saturated fatty acids (SFA) contain no

double bonds, monounsaturated fatty acids (MUFA) contain one and polyunsaturated fatty acids (PUFA) contain two or more (see Figure1).

(Figure 1 near here)

It is widely believed that the balance of these fatty acids in the diet, whether saturated or unsaturated, influence an individuals plasma cholesterol levels in terms of pro-atherogenic low-density lipoproteins (LDL) and anti-atherogenic high-density lipoproteins (HDL) (Fletcher 2005). Both lipoproteins enable fats and cholesterol to be carried in the aqueous blood stream, in which they would not normally dissolve and are therefore vital for the body as the majority of cells use and rely upon fats to function appropriately. However, an excessive amount of LDL has been associated with CVD because of the way that these lipoproteins deposit cholesterol and fats around the body (Ballantyne and Hoogeveen 2003). One of the most common nutritional concerns regarding cheese is the association between a high content of SFA in the diet and its potential to raise plasma atherogenic LDL. Cheddar cheese for example has a high total fat content, of which 62 % of the fatty acids are SFA, 27 % are MUFA and 3 % are PUFA and therefore is often viewed as an unhealthy food choice, particularly in terms of increasing ones risk of developing CVD. As a result of the association of SFAs with CVD, UK guidelines now suggest that overall fat intake should be no more than 35% of total food energy, with no more than 10% of that energy coming from saturated fats; and the remaining 20-25% of the energy coming from mono and polyunsaturated sources (Department of Health 2004). However, a closer look at the data from where dietary guidelines develop their recommendations, in terms of fat consumption and health, does not cut such a clear picture.

The link between fatty acids and CVD comes from geographic and migration studies that show positive correlations between saturated fat consumption and incidence of CVD (Keys 1980; Kromhout *et al.* 1995). However, although these data show a correlation between SFA and CVD, they cannot prove causality. This is because the aforementioned studies are seriously confounded by other lifestyle and social risk factors for CVD, such as smoking, physical inactivity, high blood pressure, obesity and other foods that may be consumed in the diet. In fact, the largest study of fat intake in a population carried out by the Nurses' Health Study, which used a cohort of 80,082 women, only found a weak positive association between SFA intake and the risk of CVD (Hu *et al.* 1997).

There are also differences in the cholesterol-raising effects of different chain lengths of SFAs found in cheese. For example, the total plasma cholesterol raising effects of SFAs are generally greater with medium chain lengths (e.g., lauric C12:0, myristic C14:0 and palmitic C16:0) than for those with longer chain lengths (e.g., stearic acid C18:0) (German and Dillard 2006). In addition, stearic acid, which accounts for 13% of the SFA in Cheddar cheese, is rapidly converted to the MUFA oleic acid C18:1, which is considered to be one of the healthier sources of fat in the diet and is a fatty acid that is not associated with increasing CVD risk (Jakobsen *et al.* 2009). This is a particularly important point for cheddar cheese, as 55 % of all its fatty acids are shorter or longer than the plasma cholesterol raising medium chain length SFAs (see Table 1).

(Table 1 near here)

Furthermore, although cheese does contain fats that may raise total plasma cholesterol, there is evidence that indicates using total plasma cholesterol levels as a marker for increased CVD risk is too simplistic. This is because changes in the atherogenic (LDL) lipoprotein particle size and the ratio of LDL to HDL in the plasma are considered to be more specific risk factors for developing CVD than total plasma cholesterol alone (Widmaier 2006a). This is mainly because small LDL particles appear to have greater atherogenic potential than large LDL particles; and a low ratio of LDL to HDL is also associated with a lower risk of CVD. This is important for cheese consumers, as fatty acids lauric, myristic and palmitic, which are fatty acids found in cheddar cheese, may indeed raise total and atherogenic LDL cholesterol but they also increase the levels of anti-atherogenic HDL cholesterol concomitantly. This suggests that a beneficial cholesterol profile (i.e. an increase in the total HDL: cholesterol ratio) may arise from the consumption of cheese in a balanced diet (Parodi 2006). In addition, Krauss (2001) found that in a large portion of healthy individuals who had large LDL particles, a low fat, high carbohydrate diet brought about a shift to smaller atherogenic LDL particles. Dreon *et al.* (1998) showed that a diet high in medium chain SFAs, such as those found in cheese, shifted LDL particles toward a larger, less atherogenic, particle size, reducing the risk of developing CVD. These studies would therefore support the consumption of cheese as part of a healthy diet in protecting against CVD because of its potential to improve a person's lipoprotein profile. However, other lipids found in cheese, such as cholesterol, have also been associated with CVD risk.

Unlike fatty acids and triglycerides, dietary cholesterol is a lipid that does not serve as a metabolic fuel. Instead cholesterol is used by the body as a precursor for cell membranes, bile salts and steroid hormones that are essential for life (Widmaier 2006b). Unfortunately cholesterol, particularly dietary cholesterol, has for many years been demonised as a lipid to be avoided in foods, in order to lower the risk of CVD. This was because cholesterol was thought to have a major influence on raising total plasma cholesterol in the blood (Fletcher *et al.* 2005). However, studies now show that the body's response to 100 mg/day of dietary cholesterol, equivalent to consuming 100g of cheddar cheese, is minimal and elevates total plasma cholesterol only very slightly, from 0.06 to 0.07 mmol/L (Parodi 2004). Furthermore, as with the SFAs, dietary cholesterol not only raises atherogenic LDL but also raises the anti-atherogenic HDL cholesterol concomitantly, such that there is little effect on the LDL: HDL ratio (McNamara 2000). Thus, it is possible for the consumption of dietary cholesterol to increase total plasma cholesterol levels without a significant change in CVD risk, because the LDL: HDL ratio remains comparatively constant. As a result the cholesterol found in cheese is unlikely to have any damaging effect on health in terms of developing an atherogenic blood profile.

Dietary guidelines concerned with linking the fat content of cheese with increasing the risk of CVD also often neglect the biological activity of individual SFAs, which potentially have important functions in the body. For example, butyric acid has been shown to regulate the expression of several genes (Smith *et al.* 1998) and may play a role in cancer prevention by halting the growth of cancer cells (German 1999); caprylic and capric acid may have antiviral activities (Thormar *et al.* 1994); lauric acid may have antiviral and antibacterial functions (Thormar and Hilmarsson 2007)

and anti-carie properties (Schuster *et al.* 1980). In addition, lipids other than SFAs found in cheese have potential biological activity.

The most recent interest in biologically active lipids from cheese has been the research into a trans-fatty acid (TFA) known as conjugated linoleic acid (CLA). The double bond of unsaturated fatty acids can exist in two stereo-isomeric forms; the cis configuration or the trans configuration (see Figure 2). Small amounts of TFAs are found in cheese because some of the PUFAs in the milk, derived from those in the animal feed, are hydrogenated by bacteria in the rumen of the cattle (Kuhlsen 2005). Other TFAs are also found in processed foods where the hydrogenation of vegetable oil is carried out industrially, for example in the manufacture of margarine (Coulate 2002). Mensink *et al.* (1998) observed that the ingestion of TFA from industrially hydrogenated vegetable oils elevated small dense LDL cholesterol and decreased HDL cholesterol and thus raised the risk of CVD. Conversely, TFA derived from ruminant sources such as CLA have been shown to be beneficial to health.

CLA was first isolated by Pariza and Hargraves (1985) from ground meat and was subsequently found to be present in dairy products derived from ruminant animals. Ever since that discovery, CLA has been keenly researched and subsequently reported to have several beneficial effects in health-related disorders when tested *in vitro* and on animals. These include anti-adipogenic (Pariza *et al.* 2001), anti-carcinogenic (Belury 2002) anti-atherogenic (Koba *et al.* 2002), anti-diabetogenic and anti-inflammatory properties (Ryder *et al.* 2001; Yang and Cook 2003); all of which have been attributed to mainly two of the twenty eight different possible CLA isomers: cis-9-trans-11 CLA and trans-10-cis-12 CLA (see Figure 2).

(Fig 2 near here)

Regrettably, CLA in cheese has for many years been considered the same as other industrial TFAs, despite the latter being considered detrimental to human health and the former potentially beneficial to human health. The failure to separate CLA in dairy products such as cheese, from industrial TFA in products such as margarine, has exacerbated negative perceptions of cheese as an unhealthy food. However, the definition of TFA was finally changed in 2004, when the Codex Committee on Nutrition and Foods for Special Dietary Uses agreed that: '… *trans fatty acids are defined as all the geometrical isomers of monounsaturated and polyunsaturated fatty acids having non-conjugated [interrupted by at least one methylene group] carbon–carbon double bonds in the trans configuration'* (CCNFSDU 2004). In other words, ruminant TFA such as CLA under this definition are no longer considered TFAs and although CLA does have a trans double bond, the double bond is conjugated (see Figure 2).

Despite the re-classification of TFA, CLAs are not explicitly excluded from the Dietary Reference Values (DRVs) recommendation that, TFA average no more than 2% of food energy intake for the population (Department of Health 2004). This is important because the DRVs set by the Department of Health are still used today as guidance values for the consumption of energy and nutrients by the British population. Furthermore, the National Diet and Nutrition Survey (NDNS), the latest survey that is used to develop nutrition policy and contributes to the evidence base for Government advice on healthy eating, does not distinguish between CLAs and

industrial TFAs either. Both government documents are important issues for the portrayal of cheese because, as with SFAs, not all TFAs in cheese are metabolically identical, as the NDNS and DRVs imply.

The majority of studies supporting CLA as a component with the potential to improve health have yet to be substantiated through human clinical trials (Wahle *et al.* 2004). However, it does draw attention to the fact that cheese contains a variety of potentially biologically active fatty acids that may have far-reaching positive health effects. These should be considered in greater detail when assessing dietary intakes of TFAs in a population or when setting out future DRV guidelines, so as to ensure physiologically beneficial foods such as cheese are not discouraged from the UK diet. Cheese consumption in the UK may also be discouraged simply because of its overall fat content regardless of the type of fat and its potential to benefit human health. This is because it is often assumed that over-consumption of fat is linked to the current global obesity epidemic, as fat has the highest energy content of all the macronutrients (Bray *et al.* 2004).

Overweight and obesity is a state of excessive body fat accumulation to an extent that increases the risk of complicating diseases such as diabetes, CVD and some forms of cancer. Body fat can be measured as the generally accepted but sometimes faulty body mass index (BMI) (weight (kg)/ height^2 (m)). A BMI between 20 and 25 indicates normal body fatness; 25-30 is the range that represents overweight and a BMI greater than 30 is a sign of obesity (WHO 1995). It is important to recognise that BMI does not account for the distribution of body fat or muscularity and can result in miss-classification of some people such as athletes and people of certain ethnicities (WHO Expert Consultation 2004). Nevertheless, overweight and obesity are growing

major health problems around the world. The WHO's latest projections indicate that in 2005 approximately 1600 million adults were overweight and at least 400 million adults were obese. It has been estimated that by 2015, approximately 2 300 million adults will be overweight and more than 700 million will be obese (WHO 2009). In the UK from 1980 to 2005, adult obesity rates quadrupled and two thirds of UK adults are now considered overweight or obese (Rennie and Jebb, 2005).

It is believed that the rise in obesity has been due to a shift towards a sedentary lifestyle combined with a diet high in energy dense foods. The amount of fat in the diet is often blamed for the increase in obesity and a number of studies support a positive association between dietary fat intake and raised body fatness (Bray *et al.* 2004; Westerterp 2006). As a result a food such as cheese, that is high in fat, is often assumed to be associated with the potential development of overweight and obesity. However, results from other studies examining the association between food composition and the extent of obesity are often conflicting.

Population studies in fact show that the increasing prevalence of obesity coincides with decreasing energy intake from fat in children and adolescents in the US (Troiano *et al.* 2000) and in Germany (Alexy *et al.* 2002). This indicates that factors other than dietary fat are involved in the global rise of overweight and obesity. Remer *et al.* (2002) and Magarey *et al.* (2001) investigated long-term nutrition of children and adolescence and could not find an independent role for fat intake and the long-term fat gain in children. Furthermore, Willet (2002) found that diets high in fat do not account for the high prevalence of people seen with excess body fat. Therefore, there is no conclusive evidence from epidemiological studies that energy derived from

dietary fat is any more hazardous than other sources of dietary energy in promoting overweight and obesity. Hence, this suggests that the consumption of high fat dairy products such as cheese is unlikely to increase body fatness any more than other types of food. In addition, the consequence of fat found in cheese on human health depends not only on the amount of fat and its bioavailability to the body but also to what extent the food is consumed and its contribution to satiety.

Cheese contributes only 6% to the average daily intake of total fat in the UK diet (Office for National Statistics 2003a). This suggests that the negative perception of cheese and the dietary guidelines that advise minimising high fat cheese consumption may be excessive and unwarranted; particularly as consumption of fat derived from cheese in the UK diet is relatively modest. Furthermore, as well as being a rich source of fat, cheese has a high content of protein, calcium and other biologically active molecules that are not only important for health but have actually been associated with the prevention of overweight and obesity (Barba and Russo 2006). Consequently, the promotion of low-fat diets by bodies such as the Food Standards Agency and the British Heart Foundation may be insignificant at best; at worst their guidelines may detract people from consuming nutritious foods that are a rich source of nutrients, because as well as being a concentrated source of fat, cheese is also a significant source of protein and essential amino acids.

Protein

Proteins are polymers of amino acids (AAs) joined together by peptide bonds and are vital for the regulation of the body's cells, tissues, and organs. The function of proteins in the body is dependent on the make up and order of the individual AAs within a protein (Nelson and Cox 2005). This dictates to what capacity the protein can

work in the body, be it an enzyme, hormone, neurotransmitter, antibody or structural component, such as tendons and ligaments. These are just a few examples of proteins, as an estimated 50 000 different proteins take part in the fundamental processes that make life possible, accounting for 17% of a person's total body mass, which underlines the importance that proteins have in maintaining human health (Kent 2000). Besides their structural and functional roles, proteins are also a fundamental component of the human diet by providing a source of energy.

Proteins in the body exist in a state of dynamic equilibrium where they are constantly being broken down and replaced. They are unique macronutrients because they are not stored in a non-functional form in the body, as are fats (in adipocytes) and carbohydrates (as glycogen) that can be hoarded awaiting use (Lee and Nieman 2007). Thus the consumption of protein is especially important for human health, as a gain or loss of protein can represent a corresponding gain or loss in body function. While the body can synthesise some AAs, others (essential AAs) must be provided by the diet. Eight AAs (leucine, isoleucine, valine, threonine, methionine, phenylalanine, tryptophan and lysine) are considered essential for adults and nine (those mentioned above plus histidine) for children (Bender and Millward 2005). In short, if the body does not receive the essential AAs it requires to build a certain protein, it will dismantle the dispensable and then the vital proteins of the body in search of the AA it requires, to the detriment of an individual's health. Thus, a continued lack of essential AAs in the diet will eventually lead to morbidity and the mortality of an individual (Sizer and Whitney 2006).

Fortunately, protein deficiency is not considered a public health issue in the UK as the average daily intake of protein is 88 g for men and 64 g for women (Office for National Statistics 2003a). This exceeds the DRVs for protein of 55.5 g d^{-1} for men aged 19-50 years and 53.3 g d^{-1} for those aged 50+ years; and 45.0 g d^{-1} for women aged 19-50 years and 46.5 g d^{-1} for those aged 50+ years (Department of Health 2004). According to the Office for National Statistics (2003a), cheese contributes approximately 5% of the total protein intake of the UK diet despite only small quantities being consumed (Women 19-64, 14 gd^{-1}; Men 19-64, 17 gd^{-1}). This is because cheese is a food of high biological value; it contains a high concentration of essential AAs and non-essential AAs derived from caseins (see Table 2).

(Table 2 near here)

Caseins are the main proteins in milk and cheese; they are a family of phosphorylated proteins (α_{S1}-, α_{S2}-, β- and κ-caseins) that combine with colloidal calcium phosphate to form aggregates known as casein micelles (Farrell *et al.* 2004). The primary function of the caseins in milk is to provide nutrients to the newborn, as they are a rich source of essential AAs, calcium and inorganic phosphate. The physico-chemical properties and much-debated loose structure of the casein micelle (McMahon and Oommen 2008), a consequence of its AA makeup, results in the casein micelles curdling when they reach the stomach, allowing them to be digested more effectively. It is merely fortuitous that the capacity of milk to form a curd is also the fundamental process involved in cheese-making. Consequently, the nutritious casein micelles that deliver nutrition and health to the mammalian neonate via milk are also a major nutritional component of cheese. Indeed, some of the proteins in cheese are more readily digestible than milk proteins as they are already partially hydrolysed during

cheese ripening to smaller peptides and amino acids (McSweeney 2004). Moreover, some of these amino acids and peptides are more than just nutritional components to be used as building blocks for proteins or as a source of energy in the body but they display biological activity too.

Peptides (fragments of proteins that contain a sequence of AAs) and free AAs arise in cheese as a result of proteolytic action from a number of proteases and peptidases that catalyse the breakdown of proteins in cheese during ripening (FitzGerald and Meisel 2003). This process is very important as it contributes directly to the flavour and texture of a cheese. The degree to which proteolysis occurs depends on a number of factors, such as the heat treatment of milk, i.e. pasteurisation, the type of coagulant used, e.g. animal or vegetable rennet, curd handling, the starter culture used, i.e. lactic acid bacteria, and the conditions under which the cheese is left to mature, e.g. time, temperature, humidity; all these factors are determined by the recipe for a particular cheese (European Food Safety Authority 2009). In addition to the importance of proteolysis for the sensory characteristics of a cheese, bioactive peptides (BPs) are also produced. This is an area of great interest because BPs may have regulatory functions in the human body that go beyond normal nutrition (Korhonen 2009).

Under *in vitro* conditions, Parrot *et al.* (2003) demonstrated that BPs are not only released during the maturation of a cheese but that they could also be liberated in the gastrointestinal tract upon the digestion of cheese. This is supported by a large number of studies reviewed by Korhonen and Pihlanto (2006) who confirmed that hydrolysis of cheese proteins by digestive enzymes can produce BPs. However, the activity of BPs is based on their AA composition, sequence and their ability to reach a

target site. Therefore, BPs must also be able to resist further degradation to inactive fragments *in vivo* in order to generate a physiological response. This was shown to be possible by a number of studies reviewed by Phelan *et al.* (2009) whereby BPs containing AAs proline and hydroxyproline were shown to be resistant to degradation by digestive enzymes. Furthermore, the transport of BPs into the circulation can depend on the size of the peptide (predominantly 2 to 50 AA residues),the charge, the molecular weight, hydrogen bonding and the hydrophobicity of the BP (Sienkiewicz-Sz1apka *et al.* 2009). This is important because BPs that can enter the circulation are then able to produce systemic effects which may have numerous physiological functions within the body. These include modulation of gut secretion and motility, blood pressure-lowering, antithrombotic, antioxidant, antimicrobial and immuno-modulatory activities. Furthermore, individual BPs have been shown to carry out more than one physiological function. FitzGerald and Meisel (2003) found peptides from ß-casein (between AAs 60 to 70) show immuno-stimulatory, opioid and angiotensin I converting enzyme (ACE) inhibitory activities. This is particularly interesting for cheese and its perception amongst the public and its place in dietary guidelines, as some of these bioactive functions are antagonistic to the non-communicable diseases commonly associated with cheese; and may actually help reduce the current rise of obesity and CVD in the UK if consumed as part of a balanced diet.

Depending on their biological effect, BPs are classified as casomorphins, ACE-inhibiting peptides, phosphopeptides, immunopeptides, antithrombotic or antimicrobial peptides (Butikofer *et al.* 2007). Gagnaire *et al.* (2001) identified a total of 28 peptides in Emmental cheese that showed immuno-stimulatory and

antimicrobial activities *in vitro* and Singh *et al.* (1997) and Ardo *et al.* (2007) isolated and identified a number of phosphopeptides derived from α_{s1}- and *ß*-casein fragments from Cheddar cheese and Herrgard cheese respectively. Phosphopeptides are important peptides because they have the ability to bind and solubilise minerals aiding their absorption in the intestine (Silva and Malcata 2005). However, ACE-inhibiting peptides make up the majority of the BPs detected and investigated in cheese. ACE inhibition is particularly important because it leads to a decrease in the level of vasoconstrictory peptide (angiotensin II) and a corresponding increase in the level of the vasodilatory peptide (bradykinin) that results in a reduction in blood pressure, an important risk-lowering factor for CVD (Fitzgerald and Murray 2006). Smacchi and Gobbetti (1998) isolated ACE inhibitory peptide fractions with varying strengths, shown in brackets, from a number of Italian cheeses, Crescenza (37% inhibition), Mozzarella (59% inhibition), Gorgonzola (80% inhibition) and Italico (82% inhibition) which showed that many cheeses have the potential to lower blood pressure and as a result, CVD risk.

Butikofer *et al.* (2007) investigated 44 hard, semi-hard and soft cheese samples of Swiss origin for the occurrence of two tri-peptides (valyl-prolyl-proline and isoleucyl-prolyl-proline) that were identified as BPs responsible for an ACE-inhibitory effect. High concentrations of the two bioactive tri-peptides often occurred in long-term ripened cheeses made from raw milk such as Emmental and Gruyere, whereas cheeses made from pasteurised milk and all soft cheeses contained only low concentrations of these BPs. However, Gomez-Ruiz *et al.* (2002) found that fifteen-day old Manchego cheese, which is prepared from sheep milk, did show high levels of ACE-inhibitory activity. This could be because ACE-inhibitory activity of a cheese increases as

proteolysis occurs during cheese maturation but then decreases when proteolysis goes beyond a certain level (Meisel *et al.* 1997). For example, an ACE-inhibitory peptide originating from α_{s1}-casein was detected in six-month old ripened Parmesan cheese but after 15 months of ripening the peptide sequence was further degraded and was no longer detectable (Addeo *et al.* 1992). Saito *et al.* (2000) also measured ACE-inhibitory activity in several cheese types where it was found that the highest activity was in two-year old Gouda cheese, whilst Ryhanen *et al.* (2001) showed that ACE-inhibitory peptide concentration was highest in a thirteen week old Gouda cheese. These results indicate that BPs liberated during cheese ripening can be degraded to the extent of becoming inactive fragments as a result of continued proteolysis. More recently, Ong *et al.* (2007) studied the release of ACE-inhibitory peptides in Cheddar cheese made with probiotic strains during ripening. They found that the addition of probiotic cultures was found to increase the ACE-inhibitory activity of the cheese during ripening. All of these studies suggest therefore, that controlling the maturation of cheese could be an important direction for cheese manufacturers to consider, in order to increase the concentration of BPs in cheese to the benefit of cheese consumers' health.

With regard to present knowledge, bovine milk and dairy products such as cheese are the greatest source of BPs derived from any other food product (Moller *et al*. 2008). Current information from a number of human studies (Mizuno *et al.* 2005; Sano *et al.* 2005; Jauhiainen *et al.* 2005) confirms the antihypertensive effects of milk-derived peptides. However, further studies are required to expand these initial findings. For example, once BPs extracted from cheese, purified via filtration techniques are found to have a physiological effect *in vitro* and *in vivo,* studies should then focus on the

content and bioavailability of BPs within the cheese matrix as is consumed by humans, in order to demonstrate physiological efficacy. Currently, only Festivo cheese, a low-fat hard cheese, claims to contain a high concentration of BPs but does not make any health claims (Ryhanen 2001). Despite this, BP sequences derived from cheese do have the potential to promote human health by reducing the risk of chronic diseases. Furthermore, these BPs could make a positive impact on the way the public views cheese and how dietary guidelines regarding cheese are put in place.

Minerals

The specific quantity of minerals found in cheese, as with other nutrients, differs according to the manufacturing procedure of a cheese type; for example, the method of coagulation used, the acidity of the curd used and the amount of salt and calcium chloride added will all have an effect on the mineral concentration of cheese (Lucey and Fox 1993). Cheddar cheese for example, is a good source of several minerals of which calcium, phosphorus, sodium and chloride are predominant; whilst trace elements such as zinc and potassium, also required by the body, are found in smaller amounts. Table 3 shows that a 50 g portion of Cheddar cheese can provide a significant proportion of the reference nutrient intake (RNI) for some of these minerals in the average male and female adult (19 – 50 years). This is important because the RNI represents the amount of each nutrient that is adequate to prevent deficiencies in 97.5 % of the UK population (Department of Health 2004). However, some controversy surrounds the salt content of cheese because of the association between excess sodium consumption and high blood pressure (Alderman 2006).

(Table 3 near here)

Salt

Salt can be added directly into the curd as the cheese is being made, e.g. Cheddar, or rubbed onto the outside of the cheese, e.g. some blue cheeses, or the cheese can be immersed directly in a vat of brine, e.g. Edam and Emmental, depending on the variety of cheese being made (Robinson and Wilbey 1998a). The addition of salt to a cheese curd is a central part of the cheese making process and has a major influence on cheese quality. For example, salt acts as a preservative in the cheese making process by inhibiting the growth of undesirable bacteria (Adams and Moss 2008). It also influences the activity of proteolytic and lipolytic enzymes that affect the structure and flavour of cheese (Fox *et al.* 2000). Furthermore, the addition of salt accelerates the expulsion of whey, reducing the moisture of the curd and affecting the rheology of the cheese (Fox *et al.* 2004). Ultimately, adding salt contributes directly to the flavour of cheese and thus has a major influence on attracting consumers.

Nutritionally, the sodium ions (Na^+) and chloride ions (Cl^-) that make up salt, are essential for life and have critical roles in a number of processes, such as maintaining a membrane potential, which is critical for triggering nerve impulse transmissions involved in muscle contraction and cardiac function (Morris *et al.* 2008). In addition, Na^+ and Cl^- ions also play important roles in nutrient absorption, nutrient transport and the maintenance of blood volume and blood pressure making salt an essential part of the diet (Scientific Advisory Committee on Nutrition 2003). The estimated minimum adult requirement for salt is approximately 0.5 g d^{-1} (Simpson 1988). However, the UK diet contains an excess of salt beyond any physiological need and far above the UK government recommended requirement of 6 g d^{-1} of salt per adult (Titze and Ritz 2009). The Medical Research Council showed that the UK's average

daily salt consumption in 2008 was 2.6 g d^{-1} over the RNI. This excessive intake of salt is considered a major factor for the high levels of hypertension seen in the UK.

In England and Wales, the prevalence of hypertension (classified as blood pressure ≥ 140/90 mm Hg) is 33 % for men and 28 % for women (Craig and Mindell 2006). This is significant because people with hypertension are three times more likely to develop CVD than people who are normotensive at 120/80 mm Hg (Scientific Advisory Committee on Nutrition 2003). As a consequence the cheese industry is often targeted by governing bodies such as the FSA to reduce the amount of salt found in cheese. Practically however, reducing the salt in cheese is very difficult as there are inherent problems with the structure and texture of the cheese if salt levels are greatly reduced, making an absolute reduction impossible (Fox *et al.* 2004). More importantly, the average person's daily intake of cheese in the UK is negligible (15 g d^{-1}), accounting for a mere 4 % of the total daily salt intake from all foods (Office for National Statistics 2003b). Therefore, changing the salt content of cheese is unlikely to have any real affect on the total salt consumed by the UK population. In addition, the evidence supporting the link between high salt intake and hypertension is still being challenged.

The Scottish Heart Health Study with 7 354 people, found no correlation between sodium intake and blood pressure (Smith 1988) and the Intersalt study with 10 079 people, only showed a moderate correlation between sodium intake and systolic blood pressure and found no correlation with diastolic blood pressure (Intersalt 1988). O'Brein and O'Connor (2004) also assert that high sodium intake contributes to hypertension in only a minority of individuals (20%) who are genetically salt

sensitive. Furthermore, the meta-analysis by Jürgens and Graudal (2004) showed that short-term low, *versus* a short term high sodium diet in Caucasians with normal blood pressure decreased blood pressure by only about 1 % and they concluded that; *"the magnitude of the effect in Caucasians with normal blood pressure does not warrant a general recommendation to reduce sodium intake in societies dominated by Caucasians."* Furthermore, it is widely recognised that obesity, inactivity, alcohol consumption and low intakes of potassium have a greater effect on blood pressure than high salt intakes (German *et al.* 2009). Suggestions have been made to reduce the sodium content of cheese by replacing part of the NaCl with KCl. However, this practice is limited due to the bitter, off-flavours KCl contributes to cheese if used in excess (Katsiari 1997).

The negative attention that cheese sometimes receives because of its salt content and the pressure that is placed on the cheese industry to reduce salt in cheese may be unwarranted. More importantly, until the link between salt consumption and raised blood pressure is unequivocal, overstating the effect that salt in cheese may have on an individual's health could unnecessarily dissuade people from consuming cheese as part of a balanced diet. This is undesirable since cheese is one of the most nutritiously complete foods consumed in the UK diet. In addition, cheese is a rich source of calcium, a mineral that in two meta-analyses was shown to reduce blood pressure (Allender *et al.* 1996; Bucher *et al.* 1996). Therefore, even if the link between salt consumption and hypertension was found to be conclusive, other components of cheese (e.g calcium and BPs) may modulate against potential increases in blood pressure.

Calcium and Phosphorus

Calcium and phosphorus in milk exist in different forms such as, ionic, casein-bound and colloidal (calcium phosphate). The equilibrium between them is important for the successful coagulation of curd during cheese making (Wolfschoon-Pombo 1997). Certain processes such as the cold storage of milk can deplete ionic (but not total) calcium to the detriment of curd formation. This problem may be overcome by pasteurisation immediately before cheese making and by the addition of calcium chloride (typically $\leq 0.02\%$) (Robinson and Wilbey 1998). Addition of calcium chloride is important for cheese making because it reduces the rennet coagulation time of milk, increases gel firmness, reduces the amount of rennet required and increases the concentration of calcium found in the cheese (Kruif and Holt 2006).

Cheese has a high concentration of calcium and phosphorus (see Table 3) that is particularly useful to the body, as it is digested in a form that is highly bio-available because of the complexes that are formed between calcium and the casein peptides within cheese. Such complexes maintain calcium in a soluble form and protect the calcium against precipitation in the intestine, facilitating calcium absorption (Ebringer *et al.* 2008). Furthermore, the calcium in cheese is a particularly good addition to the diet for lactose-intolerant individuals, as most varieties of cheese contain an insignificant amount of lactose, which is largely removed in the whey or metabolised during cheese maturation (Walther *et al.* 2008).

In ripened whole milk cheeses made with rennet, e.g. Cheddar, the calcium and phosphorus largely remain in the curd (Lucey and Fox 1993). For example, Cheddar cheese contains 370 mg 50 g^{-1} calcium and 252 mg 50 g^{-1} phosphorus (see Table 4). With regards to calcium, British men consume 1007 mg d^{-1} and British women

consume 777 mg d^{-1} (Office of National Statistics 2003b). This exceeds the RNI for calcium (700 mg d^{-1}) for male and female adults aged over 19 years old (Department of Health 2004). However, the NDNS also showed that a high proportion of teenage boys and girls and women aged 19–24 years failed to meet the lower reference nutrient intake for calcium which suggests that their calcium intakes were inadequate (Office for National Statistics 2003b). This is significant because the physiological functions of the body that are dependent on calcium take precedence over the calcium required for bone structure, i.e. the body will demineralise bone in order to maintain a normal level of blood calcium when calcium intake is inadequate (Theobald 2005). Therefore, a sufficient intake of calcium plays a key role in maintaining a healthy skeleton. This is particularly important for children, as a low intake of calcium during growth has implications for bone health later in life, with a greater risk of developing osteoporosis (Matkovic *et al.* 2005).

Osteoporosis is characterised by micro-architectural changes in bone tissue, loss of bone mineral and reduced strength of bone, increasing the risk of bone fracture (Javaid and Holt 2008). In the UK approximately 60,000 hip fractures, 50,000 distal radial fractures and 40,000 vertebral fractures occur annually at a yearly cost of nearly £1 700 million to the NHS (Russell *et al.* 2003). As the amount of calcium consumed in the diet influences peak bone mass (PBM), an adequate intake of calcium when growing is considered essential. This is because puberty is the critical period of bone growth where 90 % of PBM is accrued by the age of 19 years with 100 % PBM being accrued by the mid-thirties; thereafter bone mineral content declines. Therefore, amassing a higher PBM in early adulthood is likely to result in a higher bone density in old age, reducing the risk of a fracture later in life (Bonjour *et al.* 2009).

Currently 11 % of the total calcium in the adult UK diet is derived from cheese (Office for National Statistics 2003b). As cheese is a concentrated source of bio-available calcium, increasing the amount consumed in the daily diet has the potential to safeguard against osteoporosis in the future, particularly in those that consume inadequate quantities of calcium at a young age. In addition, calcium not only contributes to the formation and maintenance of strong bones but may help reduce blood pressure (Griffith 1999), aid in losing weight when combined with low-energy diets (Barba and Russo 2006) and the casein peptides that bind calcium in cheese may inhibit the formation of caries lesions through re-calcification of tooth enamel (Aimutis 2004). Therefore, as well as being a rich source of fats and proteins, cheese also provides a high concentration of bio-available minerals that can help reduce the risk of a number of diseases and ailments when consumed as part of a healthy diet.

Vitamins

Vitamins are complex organic substances that fall into two classes, fat soluble and water soluble, both of which are essential for many vital functions carried out by the body. With the exception of vitamin D, vitamins cannot be made by the body and so have to be consumed in the diet. Generally, only a few mg or µg of vitamins are needed per day but without them serious health complications can arise. As with all the nutrients found in cheese, the vitamin content is highly variable between types of cheese and within samples of the same variety of cheese. This is due to variations in the manufacturing processes, the cultures used, the conditions of the maturation period and the vitamin content of the milk (Oste *et al.* 1997).

Most of the milk fat (80%-85%) is retained in the cheese curd and with it, most of the fat-soluble vitamins (Parodi 2004). Table 4 shows that a 50 g portion of Cheddar cheese can provide the average adult (19-50 years) male and female with 28 % and 32% of the RNI for vitamin A respectively. This is important because vitamin A has a number of important functions, e.g. for a normal functioning immune system, in regulating gene expression and low-light vision (Russell 2000). Furthermore, absorption of vitamin A and other fat soluble vitamins such as vitamin D, E and K, are increased in the body by the presence of fats in the diet. This makes cheese a good vehicle to deliver vitamin A and other fat soluble vitamins when consumed in the diet alongside cheese.

(Table 4 near here)

The majority of water-soluble vitamins are lost from milk into the whey during cheese making. However, some water-soluble vitamins such as, riboflavin, vitamin B_{12}, niacin and folate remain in sufficient quantities to have a significant affect on human nutrition (see Table 4). For example, one portion of Cheddar cheese will provide the average male and female adult (19-50 years) with 80 % of the RNI for B_{12}. This is important as B_{12} and folic acid can help reduce high levels of homocysteine in blood, an AA that has been linked with CVD (Quinlivan *et al.* 2002); whilst riboflavin and niacin are important for the metabolism of carbohydrates, fats, and proteins (Powers 1999). Therefore the consumption of cheese as part of a balanced diet could play a significant role in maintaining a healthy vitamin intake in the UK population.

Conclusion

Cheese represents one of the most nutritionally complete foods in the UK diet and has the potential to make an important contribution to the health of the UK population. It provides a rich source of proteins, lipids and essential nutrients including calcium and vitamin A. Despite this, cheese continues to have an adverse nutritional image, largely due to the perceived association between SFA, cholesterol and the salt content of cheese with CVD. Furthermore, dietary recommendations, which promote reducing full fat cheese consumption, have often been based on equivocal positive correlations between fat consumption and CVD. Although this review recognises that some fatty acids within cheese may elevate LDL-cholesterol levels, an accepted risk factor for CVD, the effect is balanced by a concomitant increase in anti-atherogenic HDL-cholesterol levels. Furthermore, SFAs in cheese reduce the levels of atherogenic small dense LDLs and produce a larger, less atherogenic LDL particle size. In addition, certain fats, e.g. CLAs, minerals, e.g calcium, proteins, e.g BPs, and vitamins, e.g. B_{12} and folic acid, within cheese have the potential to exert beneficial metabolic effects, some of which may be cardio-protective. Regrettably, contentious dietary recommendations have been repeated so often that the association between cheese and CVD is still mistakenly perceived as fact. Consequently, people are likely to be put off from eating cheese as part of their diets. Although it should be made clear that the nutritional qualities of any food should be considered from the viewpoint of overall dietary intake and the lifestyle of a person, inclusion of cheese as part of a balanced diet is more likely to assist rather than hinder wellbeing, particularly in groups who may be consuming inadequate quantities of calcium in their diets and/or are lactose intolerant.

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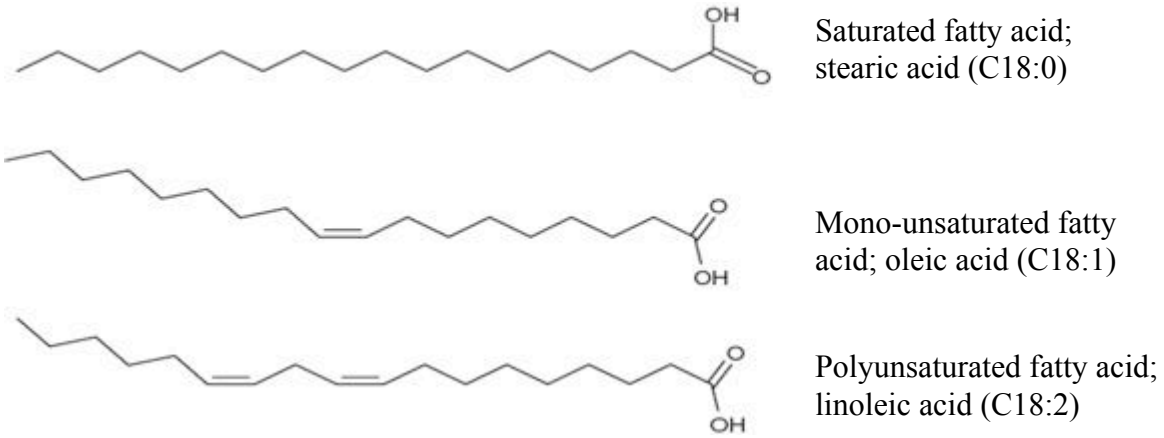

Figure 1. Basic structure of three fatty acids found in cheese.

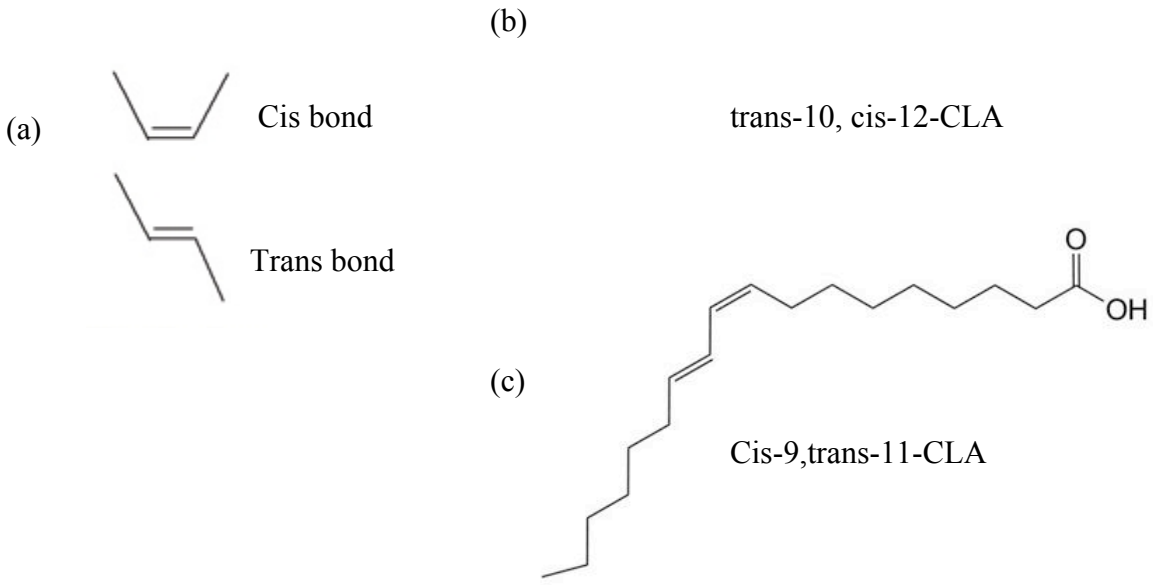

Figure 2. Chemical structures of the (a) cis- and trans- bonds and (b, c) isomers of conjugated acid (CLA).

Table 1. Major lipid content of cheddar cheese (g per 100 g cheese) (United States Department of Agriculture 2008)

Lipids	
Saturated fatty acids	grams
C4:0 Butyric	1.046
C6:0 Caproic	0.529
C8:0 Caprylic	0.279
C10:0 Capric	0.600
C12:0 Lauric	0.541
C14:0 Myrstic	3.330
C16:0 Palmitic	9.803
C18:0 Stearic	4.007
Monounsaturated fatty acids	
C16:1 Palmitoleic	1.004
C18:1 Oleic	7.905
Polyunsaturated fatty acids	
C18:2 Linoleic	0.577
C18:3 Linolenic	0.365
Other	
Cholesterol	0.105

Table 2. Typical essential (*) and non-essential amino acid content of Cheddar cheese (g per 100 g cheese) (United States Department of Agriculture 2008)

*Histidine	0.874
*Isoleucine	1.546
*Leucine	2.385
*Lysine	2.072
*Methionine	0.652
*Phenylalanine	1.311
*Threonine	0.886
*Tryptophan	0.32
*Valine	1.663
Alanine	0.703
Arginine	0.941
Cystine	0.125
Tyrosine	1.202

Table 3. Typical mineral content and the percentage of RNI derived from one portion (50g) of Cheddar cheese (Food Standards Agency 2002)

Mineral	Content per portion	Males		Females	
		RNI	% of RNI	RNI	% of RNI
Calcium (mg)	370	700	53	700	53
Sodium (mg)	362	1600	23	1600	23
Phosphorus (mg)	252	550	46	550	46
Potassium (mg)	38	3500	1	3500	1
Zinc (mg)	2	9.5	21	7	30

Table 4. Typical vitamin content and the percentage of RNI derived from one portion (50 g) of Cheddar cheese (Food Standards Agency 2002)

	Content per portion	Males		Females	
		RNI	% of RNI	RNI	% of RNI
Vitamin A (RE[1]) (µg)	194	700	28	600	32
Folate (µg)	15	200	8	200	8
Niacin (NE[3]) (mg)	3.5	17	21	13	27
B_{12} (µg)	1.2	1.5	80	1.5	80
Vitamin D (µg)	0.3	N/A	N/A	N/A	N/A
Riboflavin (mg)	0.2	1.3	15	1.1	18

[1] Retinol Equivalents (RE) represents the total vitamin A activity of cheese including β-carotene.
[3] Niacin Equivalents (NE) are estimated from both pre-formed niacin and niacin derived from tryptophan.